Summary Of Differences Between The Prior Art And The Claimed Invention Of 09/992,107

Hager (EP 0470437) (1992) • Hager discloses liposomes with a mean diameter between 50-180 nm and 70-130 nm. • Example 3 discloses liposomes with a mean diameter of 129 nm bound to propidiumiodide (a DNA marker and mutagen).	• Hager does not disclose a pharmaceutically acceptable drug free liposome preparation having the claimed Gaussian distribution. • Example 3, the only disclosure of liposomes arguably within the claimed distribution, is not pharmaceutically acceptable.
Braun (EP 0461559) • Braun discloses unilamellar liposomes having an average diameter of: • 500 nm - "several microns" (p. 1, *l.* 15*); • 60-500 nm (p. 1, *l.* 17); • 20-200 nm (p. 2, *l.* 12); • 200 nm (p. 11, *l.* 24; • below 200 nm (p. 10, *l.* 8); • 50-120 nm (p. 2, *l.* 25); • below 120 nm (p. 11, *ll.* 20-21); • 50-80 nm (p. 2, *l.* 26); • 20-50 nm (p. 1, *l.* 16); • 60 nm (p. 10, *l.* 11); • Braun teaches that the most effective liposomes are 60 nm (even though LDL increases). Data is limited to animal experiments. * (citations are to the English translation)	• Braun does not disclose a pharmaceutically acceptable liposome preparation having the claimed Gaussian distribution.

Williams 1984 [Williams et al., *Intravenously Administered Lecithin Liposomes: A Synthetic Antiatherogenic Lipid Particle*, 27.3 PERSPECTIVES IN BIOLOGY AND MEDICINE 417-431 (1984)] • Williams 1984 discloses lecithin liposomes for mobilizing cholesterol and treating atherosclerosis having diameters of 30-60 nm (page 422, *ll.* 41-43 and page 425, *ll.* 41-44). Liposomes of 21-50 nm prepared by "vigorous agitation or, more effectively, by ultrasonic irradiation" are also disclosed (p. 419, *l.* 22).	• Williams 1984 does not disclose a pharmaceutically acceptable liposome preparation having the claimed Gaussian distribution.
Williams 1986 [Williams et al., *Uptake of Endogenous Cholesterol by a Synthetic Lipoprotein*, 875 BIOCHIMICA BIOPHYSICA ACTA 183-94 (1986)] • Williams 1986 discloses liposomes that are small unilamellar vesicles that are used in animals and *in vitro* human blood samples.	• Williams 1986 does not disclose a pharmaceutically acceptable liposome preparation having the claimed Gaussian distribution.
Williams 1988 [Williams et al., *Low Density Lipoprotein Receptor-Independent Hepatic Uptake of a Synthetic, Cholesterol-Scavenging Lipoprotein: Implications For The Treatment of Receptor-Deficient Atherosclerosis, 85 Proc. Natl. Acad. Sci. 242-46 (1988)*] • Williams 1988 discloses liposomes that are small unilamellar vesicles that are used in animals.	• Williams 1988 does not disclose a pharmaceutically acceptable liposome preparation having the claimed Gaussian distribution.

Rodrigueza '93 [Rodrigueza et al., *The Influence of Size and Composition On the Cholesterol Mobilizing Properties Of Liposomes In Vivo*, 1153 BIOCHIMICA BIOPHYSICA ACTA 9-19 (July 1993)] • Rodrigueza '93 discloses the use of liposomes with a mean diameter of 70±19 nm (LUV_{50}-unilamellar), 125±30 nm (LUV_{100}-unilamellar), and 237±90 nm (MLV_{400}-multilamellar) to mobilize cholesterol from the peripheral tissues of non-atherosclerotic mice.	• This article was authored by two of the inventors and published within one year of the priority date of the present application.
U.S. Patent No. 6,139,871] • Discloses compositions and methods using unilamellar liposomes having an average diameter of 100-150 nm for treating atherosclerosis.	• This patent is not prior art because the priority date of the present application is March 4, 1994.